IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Michel H. Klein
Appl'n. No.	:	09/479,240
Filed	:	January 7, 2000
Title	:	CHIMERIC IMMUNOGENS
Grp./A.U.	:	1645
Examiner	:	Albert Mark Navarro
Docket No.	:	1038-1000 MIS:jb
Date	:	September 5, 2003

APPEAL BRIEF

BY COURIER

Mail Stop Appeal Brief-Patents
Commissioner of Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
U.S.A.

Dear Sir:

1. Introduction

This Appeal Brief, submitted in triplicate, is submitted pursuant to applicant's appeal from the Examiner's objection to the specification under 35 USC 132 as introducing new matter to the disclosure. The enclosed cheque includes the prescribed fee for an Appeal Brief.

2. Extension of Time

Petition is hereby made under provisions of 37 CFR 1.136(a) for an extension of four months of the period for filing an Appeal Brief. The enclosed cheque includes the fee for the extension of time.

3. Real Party of Interest

The real party in interest is Connaught Laboratories Limited (now Aventis Pasteur Limited) by virtue of a dead of Assignment recorded in grand-parent application No. 08/001,554 under Reel/Frame 6460/0802.

4. Related Appeals and Interferences

There are no related appeals and Interferences known to the appellant, the appellant's legal representative, or assignee which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

5. Status of Claims

Claims 1 to 58 were preliminarily deleted and new claims 59 to 76 added. Of these claims, claims 59, 61 to 70 and 72 to 74 remain pending while the remaining claims have been deleted. The pending claims have been allowed and are reproduced in the Appendix hereto.

6. Status of Amendments

An Amendment after Final Action is being submitted simultaneously herewith to correct certain clerical errors in the claims.

7. Summary of Invention

This invention relates to a multimeric hybrid gene encoding a chimeric molecule including a protein from parainfluenza virus (PIV) and a protein from respiratory syncytial virus (RSV). The hybrid gene comprises a nucleotide sequence encoding a PIV-3 HN protein or a fragment thereof having hemagglutinin-neuraminidase activity linked to a nucleotide sequence coding for a RSV F protein or a fragment thereof having fusion activity. The invention also relates to a method of preparation of the chimeric protein by expression of the multimeric hybrid gene in a cellular expression system.

8. Issues

The sole issue for determination on this appeal is the objection by the Examiner to the amendment filed January 7, 2000 under 35 USC 132 on the basis that the amendment introduces new matter into the specification. It is submitted that the objection amounts to a rejection of the claims under 35 USC 132 (or USC 112, first paragraph), since the claims include the RSV F protein depicted in Figure 5.

9. Grouping of Claims

All claims stand or fall together.

10. Argument

Figures 5A to 5E show the nucleotide sequences and deduced amino acid sequences for the respiratory syncytial virus fusion (RSV F) protein. Shortly after the grand-parent application was filed, it was discovered that, in preparing the Figure, certain nucleotides, at positions 540 and 630, were transcribed in error. A Preliminary Amendment was submitted with this application to correct these errors in Figure 5B.

The change of "T" to "C" at position 540 leads to a change of the complementary nucleotide from "A" to "G". The change of "G" to "A" at position 630 leads to a change in the complementary nucleotide "C" to "T". This change also leads to a change of the amino acid encoded by the codon including position 640 from "ARG" to "GLN".

Thus, applicants seek to change the identification of two nucleotides, the other changes being consequential on the change of identification of the two nucleotides.

The errors are clerical in nature, arising from transcription of the sequences for inclusion in the grand-parent application. It has always been possible to correct clerical errors in patent specifications and, indeed, Examiner's habitually ask applicants to check their specification in order to detect and correct clerical

errors. No one derives any benefit from an erroneous specification, neither applicants nor the public. The Examiner characterizes the changes that applicant has made as new matter.

The corrections sought to be made to the sequences are quite different from those decided as new matter in the *Ex parte Maizel*, 27 USPQ2d p1664 and are akin to the changes permitted in *Ex parte Marsili*, 214 USPQ204. A copy of each of these decisions is enclosed for convenience.

In *Ex parte Maizel*, the errors sought to be corrected arose in the original sequencing of the DNA coding sequence, which came to light upon resequencing. The original sequencing contained these errors which lead to frame shifting and an erroneous encoded amino acid sequence. By way of contrast, applicants had already expressed the RSV F gene and, indeed, correctly presented the sequence in the priority GB 9200117.1. A copy of that GB specification is enclosed for convenience.

It is clear that the corrections are minor, being two in number and giving rise to only a single amino acid change. The single amino acid difference is unlikely to have any affect on the functionality of the protein. As applicants state in the specification, the nucleotide sequence encoding the RSV F given in Figures 5A to 5D differs by approximately 1.8% divergence in the coding sequences resulting in eleven amino acid substitutions (square boxes in Figures 5A to 5E; page 15, lines 15 to 18) from a published sequence of the RSV F gene.

As mentioned above, the applicants were already in possession of the DNA encoding the RSV F protein at the time of filing of their priority GB 9200117.1. The nucleotide and amino acid sequences are set forth in the priority application in Figure 5 and a restriction map of the gene is shown in Figure 6 of the priority application. The same comparison analysis as is set forth in this application is set forth therein (see page 4, lines 32 to 35 and Figure 5). Figure 5 in the GB application correctly shows the sequence sought to be corrected by the Amendments made.

A scientific paper was published in the August 12, 1994 edition of Biotechnology, after the effective filing date of this application, describing the scientific work which is the basis for the patent application. A copy of the scientific paper is attached for information. In connection with that scientific paper, there was submitted to GenBank on September 23, 1993, after the effective filing date of this application, the nucleic acid and encoded amino acid sequences for the RSV F protein. A copy of the GenBank deposit is enclosed.

The sequences shown in the GenBank deposit are the same as those filed with the priority GB application and do not contain the errors present in Figure 5B and sought to be corrected. It is submitted that the sequences that form part of the GB application and the GenBank deposit constitute collateral evidence that the changes are corrections of errors. In the Advisory Action dated July 29, 2003, the Examiner comments that:

> "Applicants could just as easily discovered a sequence error in the foreign priority document and corrected them for filing of the US application."

This scenario is highly unlikely, since the GenBank deposit, made after this filing, contains the same sequences as the foreign priority document and applicant is seeking to correct the sequence presented in the application.

In addition, the specification describes the preparation of plasmid pD2RF-HN in Example 9 of the specification. Such plasmid was deposited with ATCC on December 17, 1992, before the effective filing date of this application, under accession number 75388 (see page 12, lines 27 to 43).

As described in Example 9, the RSV F gene lacking the transmembrane domain and cytoplasmic tail was linked to the PIV-3 HN gene devoid of the hydrophobic anchor domain and cloned into baculovirus expression vector pD2 to provide plasmid pD2 RF-HN. As is seen from Figure 5, the portion of the RSV F nucleotide sequence that is present in the deposited plasmid encompasses that where the corrections are sought to be made. A person

sequencing the RSV F gene from plasmid pD2 RF-HN would discover the errors in the sequences shown in Figure 5A.

As determined by the Federal Court in the *Enzo Biochem Inc. v. Gen-Probe Incorporated et al* [citation], a deposit of a biological material constitutes an adequate description of the deposited material sufficient to comply with the written description requirement of 35 USC 112, first paragraph. Accordingly, the specification as filed contains a written description of the portion of the sequence that is sought to be corrected.

The Examiner relies solely on MPEP608 for his rejection, quoting:

> "All amendments or claims must find descriptive basis in the original disclosure, or they involve new matter."

It is submitted that this statement is not intended to deal with corrections of all types, since corrections are routinely permitted by the Office.

Ex parte Maizel recognizes this principle:

> "We recognize that errors may well arise in the sequencing of DNA and that a mechanism for correcting such errors in the Patent and Trademark Office is highly desirable"

If such errors could not be corrected because of MPEP608, then there would be no need for the Board to express a desire for a mechanism of correction.

The Board goes on to state:

> "Unfortunately, no general rule can be established because the question of whether or not a change in the chemical structure of a DNA sequence set forth in the specification is permitted depends on the facts of each case and the significance of the modification to both the subject matter *claimed*, i.e., the *invention*, and the subject matter *described* in the specification." (emphasis in original)

Thus, the Board indicated there could be no general rule, but did recognize that a change to a DNA sequence may be permitted, depending on the facts of the

situation and the significance of the modification. The Board certainly did not consider that such changes to correct errors were proscribed by MPEP 608.

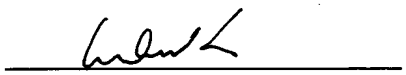
The facts surrounding the Examiner's rejection are quite different from that in *Ex parte Maizel*. In *Maizel*, the error arose in the sequencing itself, only discovered on resequencing. In this case, the sequencing had been done, as evident from the priority GB application and the error later arose in transcribing the sequence for the grand-parent application.

In *Ex parte Marsili*, the applicants were permitting to change the chemical structure of a compound as set forth in claim 1. A more refined investigation of the structure of the compound showed that a hetrocyclic ring, depicted as saturated, was unsaturated at two locations in the ring.

11. Summary

For these reasons, it is submitted that the Examiner is in error in objecting to the specification under 35 USC 132 as containing new matter and the objection, therefore, should be REVERSED.

Respectfully submitted,



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APPENDIX
CLAIMS APPEALED

59. A multimeric hybrid gene encoding a chimeric protein including a protein from parainfluenza virus (PIV) and a protein from respiratory syncytial virus (RSV), comprising a nucleotide sequence encoding a PIV-3 HN protein or a fragment thereof having hemagglutinin-neurominidase activity linked to a nucleotide sequence coding for a RSV F protein or a fragment thereof having fusion activity.

61. The hybrid gene of claim 59 contained in an expression vector.

62. The hybrid gene of claim 61 in the form of a plasmid which is pD2 RF-HN (ATCC 75388).

63. Eukaryotic cells containing the multimeric hybrid gene of claim 59 for expression of the chimeric protein encoded by the hybrid gene.

64. The cells of claim 63 which are mammalian cells, insect cells, yeast cells or fungal cells.

65. A vector for antigen delivery containing the gene of claim 59.

66. The vector of claim 65 which is viral vector.

67. The vector of claim 66 wherein said viral vector is selected from the group consisting of poxviral, adenoviral and retroviral viral vectors.

68. The vector of claim 65 which is a bacterial vector.

69. The vector of claim 68 wherein said bacterial vector is selected from salmonella and mycobacteria.

70. A process for the preparation of a chimeric protein including a protein from parainfluenza virus (PIV) and a protein from respiratory syncytial virus (RSV), which comprises:

isolating a first nucleotide sequence encoding a PIV-3 HN protein or a fragment thereof having hemagglutinin-neurominidase activities,

isolating a second nucleotide sequence encoding a RSV F protein or a fragment thereof having fusion activity,

linking said first and second nucleotide sequences to form a multimeric hybrid gene, and

expressing the multimeric hybrid gene in a cellular expression system.

72. The process of claim 70 wherein said multimeric hybrid gene is contained in an expression vector which is pD2 RF-HN (ATCC 75388.

73. The process of claim 70 wherein said cellular expression system is provided by mammalian cells, insect cells, yeast cells or fungal cells.

74. The process of claim 70 including separating a chimeric protein from a culture of said eukaryotic cellular expression and purifying the separated chimeric protein.